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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

THOMAS, TIMOTHY P

ART UNIT	PAPER NUMBER
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1614

NOTIFICATION DATE	DELIVERY MODE
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04/23/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/584,445	Applicant(s) LEVERD ET AL.	
	Examiner TIMOTHY P. THOMAS	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12-16 is/are pending in the application.
- 4a) Of the above claim(s) 10, 12 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 13-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 June 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>10/4/2006; 1/22/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-9 and 13-15 in the reply filed on 1/28/2008 is acknowledged. The traversal is on the ground(s) that the newly introduced limitation of the claim amendment (the composition does not contain any preservatives) is no longer obviated by the references previously cited. This is not found persuasive because the claims as filed were obvious for the reason of record. Additionally, the rejections that appear below demonstrate that the amended claims still lack inventive step; the requirement is maintained. Applicant also requests that claim 12 is rejoined, since the claim includes all of the composition features of claim 1. Claim 12 contains features and steps not required by claim 1, such as an inert nitrogen atmosphere and successive steps that are not necessary to produce the composition of claim 1; the requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 10, 12 and 16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/28/2008.

Drawings

3. The drawings are objected to under 37 CFR 1.83(a) because they fail to show all 7 sets of data named in the key and described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown

in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

4. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Content of Specification

- (a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

- (b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.
- (c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.
- (d) The Names Of The Parties To A Joint Research Agreement: See 37 CFR 1.71(g).
- (e) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.
- (f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:
 - (1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."
 - (2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."
- (g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the

invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

- (h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.
- (i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.
- (j) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).
- (k) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).
- (l) Sequence Listing. See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

5. The disclosure is objected to because of the following informalities: the specification does not contain a section, "Brief Description of the Drawing" (Item (h) above).

Appropriate correction is required.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1-3, 7, 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over GlaxoSmithKline ("Prescribing Information: Navelbine (vinorelbine tartrate) Injection: 2002 Nov; pp. 1-17; IDS 1/22/2008 reference CA) and Duflos et al. (US 6,127,377; 2000; IDS 10/4/2006 reference AB).

10. GlaxoSmithKline teaches vinorelbine tartrate aqueous solutions that are sterile and nonpyrogenic, and containing no preservatives or other additives (p. 1, Description section, 1st paragraph); the name and structure show a 1:2 vinorelbine:tartrate salt (ditartrate; p. 1, Description section, 2nd paragraph; structure); the composition consists of the vinca alkaloid compound in distilled water for injection at a concentration of 10 mg/mL, for which the pH is about 3.5 (p. 1, Description section, 1st, 2nd & 4th paragraphs) the solutions are supplied in single-use clear glass vials, individually packaged in a carton (a packaging container; p. 17, 1st paragraph). GlaxoSmithKline does not teach vinflunine ditartrate compositions. Duflos teaches novel halogenated derivatives of the vinorelbine family and therapeutically acceptable salts, specifically vinflunine (abstract) and vinflunine ditartrate (col. 13, line 42); the compounds have characteristic pharmacological properties of vinca alkaloids, i.e., inhibition of polymerization of tubulin into microtubules, and are thus useful in anticancer therapy (col. 13, line 50-col. 14, line 12); compositions that contain an active compound and a pharmaceutically acceptable vehicle are taught (claim 9). It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute vinflunine

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ditartrate at 10 mg/ml vinflunine for vinorelbine tartrate in the aqueous solutions taught by GlaxoSmithKline giving the compositions of the instant claims. The motivation would have been the substitution of one art-recognized equivalent vinca alkaloid with anticancer properties (vinflunine ditartrate) for another (vinorelbine tartrate). Dissolution of vinflunine ditartrate into distilled water inherently gives a pH of about 3.5 and stability of solutions for 36 months, as disclosed by applicant (specification, p. 13, lines 1-3, 17-20).

11. Claims 1-2, 4-7, 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolgemuth (CA-2,001,643; 1990; IDS 10/4/2006 reference BC) and Duflos et al. (US 6,127,377; 2000; IDS 10/4/2006 reference AB).

Wolgemuth teaches preservative-free, sterile, stable, multiple dose solutions of a vincristine salt for intravenous use, with concentrations of 0.50-2.0 mg/mL (title; abstract); a pH range from about 3.5 to about 5.5, preferably 4.0-4.5 (p. 2, lines 16-17; claim 10); buffers include acetic acid/sodium acetate at 0.2 M (p. 4, line 34; p. 7, lines 5-6); solutions are stored in multiple dose containers (packaging container; claim 10). Wolgemuth does not teach solutions with vinflunine ditartrate; the pH ranges overlap with the instant claims. Duflos teaches novel halogenated derivatives of the vinorelbine family, including vincristine and therapeutically acceptable salts, specifically vinflunine (abstract; col. 1, line 45) and vinflunine ditartrate (col. 13, line 42); the compounds have characteristic pharmacological properties of vinca alkaloids, i.e., inhibition of polymerization of tubulin into microtubules, and are thus useful in anticancer therapy (col. 13, line 50-col. 14, line 12); compositions that contain an active compound and a

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pharmaceutically acceptable vehicle are taught (claim 9). It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute vinflunine ditartrate at 0.5-2 mg/ml vinflunine for a vincristine salt in the aqueous solutions taught by Wolgemuth giving the compositions of the instant claims. The motivation would have been the substitution of one art-recognized equivalent vinca alkaloid with anticancer properties (vinflunine ditartrate) for another (a vincristine salt). It would also have been obvious to optimize the pH range for the stability of the vinflunine ditartrate solutions, which would have given pH values within the range of the instant claims. Absent evidence to the contrary, dissolution of vinflunine ditartrate into an aqueous solution as taught by Wolgemuth, would inherently be stable for 36 months, as disclosed by applicant (specification, p. 13, lines 17-20).

12. Claims 8 and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over GlaxoSmithKline ("Prescribing Information: Navelbine (vinorelbine tartrate) Injection: 2002 Nov; pp. 1-17; IDS 1/22/2008 reference CA); Duflos et al. (US 6,127,377; 2000; IDS 10/4/2006 reference AB); and Wolgemuth (CA-2,001,643; 1990; IDS 10/4/2006 reference BC) as applied to claims 1-3, 7, 9 and 13; and 1-2, 4-7, 9 and 13 above, and further in view of Howell et al. ("Anti-vascular effects of vinflunine in the MAC 15A transplantable adenocarcinoma model"; 2001; British Journal of Cancer; 84(2): 209-295; IDS 10/4/2006 reference CG).

GlaxoSmithKline teaches solutions of 10mg/mL and 50mg/5mL (p. 17, 1st paragraph) and that vinorelbine is soluble greater than 1000 mg/mL. Wolgemuth teaches vincristine solutions at 0.50-2.0 mg/mL (abstract). None of GlaxoSmithKline,

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Wolgemuth or Duflos teach 50mg/2mL or 100 mg/100mL or 250 mg/250mg/4mL of base vinflunine or other vinca alkaloid nor concentrations between 25-30 mg/mL or 25 mg/mL, required by the instant claims. Holwell teaches the maximum tolerated dose for vinflunine is 50 mg/kg and for vinorelbine is 8 mg/kg (i.e., 6.25 times the dose of vinflunine with respect to vinorelbine is the maximum tolerated); vinflurine produced anti-vascular effects at doses much lower than the maximum tolerated dose. Therefore it would have been obvious to increase the amounts of vinflunine as compared to the vinorelbine or vincristine solutions and to optimize the amounts, giving the concentrations of the instant claims. The motivation for routine optimization of the invention would have been the ability for individuals to tolerate higher doses of vinflurine and the potential enhancement of anti-cancer therapy.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614